REMARKS

The Claims

Claims 62, 64, 69-71, 76, 82, 83 and 85 have been amended to correct minor informalities and/or to more particularly point out and distinctly claim certain subject matter. Claims 63, 64, 66, 69-75, 77-80, and 82-84 have been amended to provide appropriate dependency and remove dependencies on cancelled claims. No new matter has been added.

Claims 65, 67, 68, and 81 have been cancelled without prejudice or disclaimer.

Now pending in the application are claims 62-64, 66, 69-80, and 82-85.

Rejection under 35 U.S.C. §112, second paragraph

Claims 63-75 and 77-84 were rejected under 35 U.S.C. §112, second paragraph, as allegedly unclear. This rejection is traversed.

As noted above, the claims have been amended to provide appropriate dependencies and to correct minor informalities. Applicant respectfully contends that the pending claims are not unclear or indefinite. Reconsideration and withdrawal of the rejection is proper and the same is requested.

Rejection under 35 U.S.C. §103(a)

Claims 62-85 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Crenshaw et al. (U.S. Patent No. 5,151,448), Krushinski et al.(U.S. Patent No. 5,576,321), in view of Smith et al. (U.S. Patent No. 6,037,360) and Grass et al. (U.S. Patent No. 6,542,858) and Bick (U.S. Patent No. 4,940,731) in view of Hirai et al. (U.S. Patent No. 4,659,696), Uda et al. (U.S. Patent No. 4,670,419), and Rubsamen et al. (U.S. Patent Publication No. 2004/0208829). This rejection is traversed.

Crenshaw teaches that premature ejaculation in male humans patients can be effectively treated by the administration, preferably oral, of a fluoxetine dose effective to delay the onset of ejaculation during subsequent sexual intercourse (see, e.g., column 1, lines 49-52). Although Crenshaw discloses that other routes of administration e.g., parental, by suppositories, buccal dosage forms, skin patch, and the like, can also be

utilized (see, e.g., column 2 lines 66-68), Crenshaw does not teach or disclose any form of administration other than by administration via a single route. In particular, Crenshaw teaches that oral administration is the preferred route of administration (column 1, lines 58-59). Crenshaw does not teach or disclose a method of administering an antidepressant to a male via a combination of two independent routes for treating premature ejaculation in a male, as required by the pending claims. Moreover, Crenshaw does not teach or disclose administration of an antidepressant via a combination of mucosal administration and local administration to at least part of the male genitalia, as recited in the pending claims.

Crenshaw teaches that the active ingredient in the individual dosage forms can be combined with the conventional pharmaceutical excipients and formed into tablets, capsules, and the like (Column 2, line 68 - Column 3, line 3). Crenshaw further teaches that for chronic administration of the active ingredient, oral dosage forms are preferred (Column 3, lines 7-8). Crenshaw therefore teaches away from the presently-claimed subject matter.

Krushinski teaches of a series of hetero-oxy alkanamines for the treatment of conditions related to or affected by the reuptake of serotonin and by the serotonin 1_A receptor (see, e.g., the Abstract). These compounds may be administered in an adjunctive therapy with a serotonin reuptake inhibitor (SRI) (see, e.g., Column 115, lines 32-34). Krushinski further teaches that all the compounds concerned are orally available and are normally administered orally, and so oral administration of the adjunctive combination is preferred (Column 115, line 34-38).

Although Krushinski teaches that one of the drugs may be administered by one route, such as oral, and the other may be administered by the transdermal, percutaneous, intravenous, intramuscular, intranasal or intrarectal route (column 115, line 44-47), Krushinski does not teach or disclose that the SRIs are to be administered via separate routes. Neither Crenshaw nor Krushinski, taken separately or in combination, teaches or discloses a method of administering an antidepressant to a patient via a combination of two independent routes for treating premature ejaculation in a male.

Smith cannot remedy the deficiencies of the Crenshaw and/or Krushinski references. Smith teaches that a selected pharmacologically active agent is administered to an individual with a history of premature ejaculation. The active agent may be administered orally, parenterally, bucally, rectally, or locally by intracavernosal injection or by delivery to the urethra (Column 5, line 2-7). The pharmaceutical compositions according to Smith may also be administered by nasal aerosol or inhalation (Column 9, lines 36-38). Smith however, does not teach or disclose a method of administering an antidepressant to a patient via a combination of two independent routes for treating premature ejaculation in a male. Smith also does not teach or disclose a composition for the treatment of premature ejaculation comprising an antidepressant formulated for mucosal administration and for local administration to at least part of the male genitalia. Smith merely teaches that drug delivery may be accomplished through any route effective to provide relief from premature ejaculation, including oral, parenteral, buccal, rectal, topical, transdermal, transurethral, and intracavernosal (column 3, lines 25-30). Smith is completely silent as to the benefits of administering an antidepressant to a male via a combination of mucosal administration and local administration to at least a part of the male genitalia. Although Smith discloses a kit which may be used to assist an individual in administering a drug to treat premature ejaculation, Smith does not teach or disclose a kit comprising an antidepressant formulated for nasal administration and an antidepressant formulated for local administration to at least part of the male genitalia, as presently claimed in claim 85.

The Grass patent also cannot remedy the deficiencies of the Crenshaw and/or Krushinski references (or the remaining cited references). The Office Action states that Grass teaches "pharmacokinetic modeling of the dosage forms as disclosed," but Grass does not teach or suggest the specific combination of routes of administration of the subject matter as presently claimed.

It is unclear whether the Bick, Hirai, Uda, and Rubsamen references are applied to some or all of the pending claims. To ensure a complete response, Applicant contends that none of these patents, alone or in combination, remedy the deficiencies of the Crenshaw and/or Krushinski references. With respect to the rejection of claims

82-83, the Office Action states that Hirai teaches pharmaceutical compositions for nasal or vaginal use. However, the Office Action does not allege that Hirai teaches or suggests the specific combination of routes of administration of the subject matter as presently claimed. The Office Action does not provide any discussion at all of the Bick, Uda, and Rubsamen references. Thus, none of these references, alone or in combination with Crenshaw, Krushinski, Smith, Grass and/or Hirai, can render obvious the claimed subject matter.

As described in the present specification at page 14, lines 13-16, all three routes of administration (oral, nasal, and a combination of topical and nasal) were found to produce a reduction in premature ejaculation as a whole. Surprisingly however, those subjects taking the antidepressants by both nasal administration and local administration to at least a part of the male genitalia noted particularly good results (Specification, page 15, lines 4-6).

It will be appreciated by one of skill in the art that the treatment of premature ejaculation and the consequent prolonging of sexual intercourse does not readily lend itself to objective qualification, but rather needs to be assessed by feedback to the clinician by the patient which is necessarily both subjective and qualitative. As described in the present specification, the combination of nasal and topical administration to the male genitalia provided the best results to the largest number of subjects. This is clearly demonstrated in the table at page 15, as discussed above. As described at the last paragraph on page 14 of the present specification, in excess of 200 patients were tested for each administration route, plus 200 patients for the combination route (nasal plus topical) as presently claimed. Patients showed a positive assessment of their sexual satisfaction for each of the tested routes of administration; however, when nasal plus topical administration was used, the patients as a whole were, subjectively, more satisfied.

The method of treating premature ejaculation in a male comprising administering to the male an antidepressant via a combination or mucosal administration and local administration to at least a part of the male genitalia has surprisingly led subjects to experience the greatest reduction in premature ejaculation as a whole. The combination

of mucosal, preferably nasal, and local administration has been found to be extremely useful in preventing premature ejaculation and prolonging sexual intercourse.

None of the cited references teaches or discloses, either alone or in any combination, a method of treating premature ejaculation in a male comprising administering to the male an antidepressant via a combination of mucosal administration and local administration to at least a part of the male genitalia, as claimed in pending claim 62 (and claims dependent therefrom). The cited references also neither teach nor disclose, either solely or collectively, a composition for the treatment of premature ejaculation comprising an antidepressant formulated for mucosal administration and for local administration to at least a part of the male genitalia, as claimed in pending claim 76 (and claims dependent therefrom), nor a kit comprising an antidepressant formulated for nasal administration and an antidepressant formulated for local administration to at least part of the male genitalia, as claimed in pending claim 85.

Claims 82 and 83 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Crenshaw et al. (U.S. Patent No. 5,151,448), Krushinski et al.(U.S. Patent No. 5,576,321), in view of Smith et al. (U.S. Patent No. 6,037,360) and Grass et al. (U.S. Patent No. 6,542,858) and further in view of Hirai et al. (U.S. Patent No. 4,659,696). This rejection is traversed.

The teachings of each of these references have been described above. Applicant respectfully submits that none of the references, alone or in any combination, teaches or suggests the subject matter of the claims 82 and 83. For example, the references do not teach or suggest a composition formulated for administration by the specific combination of routes as recited by claims 82 and 83.

In summary, Applicant contends that none of the cited references, whether taken alone or in any combination, can render obvious the subject matter of the pending claims. Reconsideration and withdrawal of the rejections is proper and the same is requested.

CONCLUSION

For at least the foregoing reasons, all claims of this application are deemed to be in condition for allowance, and allowance is accordingly requested. However, if the Examiner considers that obstacles to allowance remain, the Examiner is invited to contact the undersigned.

Applicant requests any extension of time necessary for consideration of this response. If for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105**, under Reference No. 64734 (70403), Customer No. 21874.

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Respectfully submitted,

By: /Mark D. Russett/
Mark D. Russett, Reg. No.: 41,281
Jeffrey D. Hsi, Reg. No.: 40,024
EDWARDS ANGELL PALMER & DODGE LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 239-0100
Attorneys/Agents For Applicant